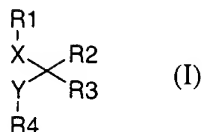


CLAIMS

Amn.
a¹

1. A compound of general Formula I



5 or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, wherein

R₁ represents,

C₁-C₆ alkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

10 cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

heterocyclyl, containing at least one nitrogen atom;

heterocyclyl, containing at least one hetero atom selected from S or O,

15 and substituted with one or more basic groups such as amino, amidino and/or guanidino;

or aryl, substituted with one or more basic groups such as amino, amidino and/or guanidino,

R₂ represents H, acyl, acylamino, alkyl, alkylcarbonyl, alkylthio, alkoxy, aroyl,

20 aroylamino, aryloxy, arylthio, amidino, amino, aryl, carbonyl, carboxy, cyano, cycloalkyl, formyl, guanidino, halogen, heterocyclyl, hydroxy, oxo, nitro, thiol, Z₂N-CO-O-, ZO-CO-NZ- or Z₂N-CO-NZ- group,

R₃ represents COOR₅, SO(OR₅), SO₃R₅, P=O(OR₅)₂, B(OR₅)₂, P=OR₅(OR₅), or tetrazole, or any carboxylic acid isostere,

25 R₄ represents SH, S-CO-C₁-C₆ alkyl or S-CO-aryl,

R₅ represents H, C₁-C₆ alkyl or aryl,

R₆ represents H or C₁-C₆ alkyl,

X represents O, S, SO, SO₂, C(Z)₂, N(Z), NR₆SO₂, SO₂NR₆, NR₆CO or CONR₆,

Y represents C(Z)₂,

contd.
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~~X represents independently H, C₁-C₆ alkyl, aryl, cycloalkyl or heterocyclyl.~~

~~2. The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,~~

~~5 wherein~~

~~R₁ represents,~~

~~cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or~~

~~guanidino;~~

~~heterocyclyl, containing at least one nitrogen atom;~~

~~10~~

~~heterocyclyl, containing at least one hetero atom selected from S or O, and substituted~~

~~with one or more basic groups such as amino, amidino and/or guanidino;~~

~~or aryl, substituted with one or more basic groups such as amino, amidino and/or~~

~~guanidino;~~

~~R₂ represents H, acyl, acylamino, alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl,~~

~~15~~

~~aroylamino, aryloxy, arylthio, amidino, amino, aryl, carbamoyl, carboxy, cyano,~~

~~cycloalkyl, formyl, guanidino, halogen, heterocyclyl, hydroxy, oxo, nitro, thiol, Z₂N-~~

~~CO-O-, ZO-CO-NZ- or Z₂N-CO-NZ- group,~~

~~R₃ represents COOR₅,~~

~~R₄ represents SH, S-CO-C₁-C₆ alkyl or S-CO-aryl,~~

~~20~~

~~R₅ represents H, C₁-C₆ alkyl or aryl,~~

~~R₆ represents H or C₁-C₆ alkyl,~~

~~X represents O, S, SO, SO₂, C(Z)₂, N(Z), NR₆SO₂, SO₂NR₆, or CONR₆,~~

~~Y represents C(Z)₂,~~

~~Z represents independently H, C₁-C₆ alkyl, aryl, cycloalkyl or heterocyclyl.~~

~~25~~

~~3. The compound according to claim 1 or 2, or a pharmaceutically acceptable salt or~~

~~solvate thereof, or a solvate of such a salt,~~

~~wherein~~

~~R₁ represents,~~

~~30~~

~~cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or~~

~~guanidino;~~

~~heterocyclyl, containing at least one nitrogen atom~~

contd.
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heterocyclyl, containing at least one hetero atom selected from S or O, and substituted with one or more basic groups such as amino, amidino and/or guanidino;

R₂ represents H, C₁-C₃ alkyl, amino, halogen, hydroxy,

R₃ represents COOR₅,

5 R₄ represents SH, S-CO-C₁-C₆ alkyl or S-CO-aryl,

R₅ represents H, C₁-C₆ alkyl or aryl,

X represents C(Z)₂,

Y represents C(Z)₂,

Z represents independently H or C₁-C₆ alkyl.

10

4. The compound according to any previous claim, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, wherein

R₁ represents,

15 cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

heterocyclyl, containing at least one nitrogen atom;

R₂ represents H, F, or C₁ alkyl,

R₃ represents COOR₅,

20 R₄ represents SH, S-CO-C₁-C₆ alkyl or S-CO-aryl,

R₅ represents H, C₁-C₆ alkyl or aryl,

X represents C(Z)₂,

Y represents C(Z)₂,

Z represents independently H or C₁-C₆ alkyl.

25

5. The compound according to any previous claim, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, wherein

R₁ represents cyclopentyl, pyridyl, pyrimidinyl, piperidinyl or thiazolyl,

R₂ represents H, F, or C₁ alkyl,

30 R₃ represents COOR₅,

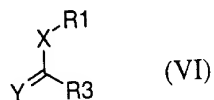
R₄ represents SH,

R₅ represents H,

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Q1*

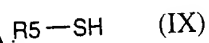
X represents CHZ,
Y represents CHZ,
Z represents independently H or C₁-C₆ alkyl.

- 5 6. A process for the preparation of a compound according to any one of claims 1-5,
wherein R₁, R₃, R₄, and Y are as defined in claim 1 and X is C(Z)₂ and R₂ is H, comprising
the step of;
reacting a compound of Formula VI,



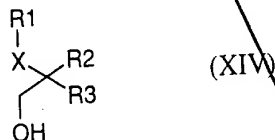
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wherein R₁, R₃ and Y are as defined in claim 1 and X is C(Z)₂, with a compound of
Formula IX,

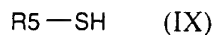


- 15 wherein R₅ is a suitable protecting group, such as Ac, Bz, PMB or Bn, alone or in the
presence of a suitable base, such as NaOMe, NaH or triethylamine or alternatively in the
presence of a free-radical initiator, such as AIBN under standard conditions.

7. A process for the preparation of a compound according to any one of claims 1-5,
wherein R₁, R₂, R₃, and R₄ are as defined in claim 1 and Y is CH₂ and X is O, S, C(Z)₂, or
20 N(Z), comprising the step of:
reacting a compound of Formula XIV,



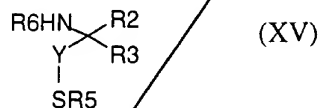
wherein R_1 , R_2 , and R_3 are as defined in claim 1 and X is O, S, $C(Z)_2$, or $N(Z)$, with a compound of general Formula IX,



wherein R_5 is a suitable protecting group, such as Ac or Bz, in the presence of a suitable reagent, such as PPh_3 /DIAD, under standard conditions.

8. A process for the preparation of a compound according to any one of claims 1-5, wherein R_1 , R_2 , R_3 , R_4 , and Y are as defined in claim 1 and X is NR_6CO , or NR_6SO_2 comprising the step of:

10 reacting a compound of the general Formula XV,



wherein R_2 , R_3 , R_6 and Y are as defined in claim 1 and R_5 is a suitable protecting group, such as Ac, Bz, PMB or Bn, with a compound of the general Formula XVI,



15 wherein R_1 is as defined for in claim 1 and X is $COOH$ or SO_2Cl in the presence of suitable coupling reagents, such as PyBOP/DIPEA, DCC/HOBt, EDC/TEA/DMAP or pyridine, under standard conditions.

20 9. A pharmaceutical formulation containing a compound according to any one of claims 1 to 5 as active ingredient in combination with a pharmaceutically acceptable adjuvant, diluent or carrier.

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~~10. The use of a compound according to any one of claims 1 to 5 in therapy.~~

11. The use of a compound according to any one of claims 1 to 5 for the manufacture of a ~~medicament~~ for the inhibition of carboxypeptidase U.

Amem.
Q2 5 12. A method for treatment or prophylaxis of conditions associated with inhibition of carboxypeptidase U, comprising administering to a mammal, including man, in need of such treatment an effective amount of a compound as defined in any of claims 1-5.

10 13. A pharmaceutical formulation for use in the treatment or prophylaxis of conditions associated with inhibition of carboxypeptidase U, comprising a compound as defined in any of claims 1-5 in combination with a pharmaceutically acceptable adjuvant, diluent or carrier.

15 14. A pharmaceutical formulation, comprising:
(i) a compound of Formula I or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, and
(ii) one or more antithrombotic agent with a different mechanism of action, such as an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor or ADP-receptor (P₂T) antagonist,
20 in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

25 15. A kit of parts comprising:
(i) a pharmaceutical formulation containing a compound of Formula I, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; and
(ii) a pharmaceutical formulation containing one or more antithrombotic agent with a different mechanism of action, such as an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor or ADP-receptor (P₂T) antagonist,
30 in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

contd.
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which compound (i) and agent (ii) are each provided in a form that is suitable for administration in conjunction with the other.

16. A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of carboxypeptidase U and a different antithrombotic mechanism are required or desired, which method comprises administering to the patient a therapeutically effective total amount of

(i) a compound of Formula I, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; in conjunction with

(ii) one or more antithrombotic agent with a different mechanism of action, such as an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor or ADP-receptor (P₂T) antagonist,

in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

17. A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of carboxypeptidase U and a different antithrombotic mechanism are required or desired, which method comprises administering to the patient a formulation as defined in claim 14.

Add
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